CVGENG.007A PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Stegmann, T.	) Group Art Unit 1651
Appl. No.	:	09/358,780	)
Filed	:	July 22, 1999	)
For	:	**INDUCTION OF NEOANGIOGENESIS IN ISCHEMIC MYOCARDIUM**	)
Examiner	:	Patten, P.	

SECOND DECLARATION UNDER 37 C.F.R. § 1.131

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I Dr. Thomas Stegmann, declare as follows:

1. I am the inventor of the claims of the above-identified patent application and inventor of the subject matter described and claimed therein.

2. Prior to November 4, 1997, I had completed my invention as described and claimed in the above-referenced application in the United States or in a NAFTA or WTO country at a date prior to the date of publication of the reference: U.S. patent No. 6,045,565, filed November 2, 1998 which claims priority to Provisional application No. 60/064,210, filed November 4, 1997.

3. In the reference: Schumacher, et al. (February 24, 1998) "Induction of Neoangiogenesis in Ischemic Myocardium by Human Growth Factors" Circulation vol. 97 (7), pages 645-650, significant concepts of the invention are described, e.g. injection of human growth factor FGF-1 close to the vessels into ischemic tissue to induce neoangiogenesis and revascularization in

human subjects. The disclosure contained in the reference therefore implies a completion of the principal aspects of the invention and reduction to practice. The date of invention with respect to those concepts must necessarily precede the date the reference was submitted for publication, January 9, 1997. This reference was submitted with the Information Disclosure Statement of March 9, 2000 and is attached hereto as Exhibit A for the convenience of the Examiner.

4. However, even before the time of the Schumacher, et al. publication (Exhibit A), I had conceived the pharmaceutical composition of FGF-1 and physiologic glue for the purpose of injecting an amount of the composition into the ischemic myocardium at or near at least one predetermined site of coronary artery stenosis to induce local neoangiogenesis in connection with Claim 1 of the above-captioned patent application and was diligent in reduction to practice as shown by the Final Study Report for the FGF-1 Study (Exhibit B).

5. In the attached Final Study Report for the FGF-1 Study (Exhibit B) performed by myself, the injection of human growth factor FGF-1 with fibrin glue close to the vessels into ischemic tissue to induce neoangiogenesis and revascularization in human subjects is described. See "Methodology," page 4; "Test Product," page 5; "Conclusion," page 6; and "Treatments," page 9.

6. My method of revascularizing a region of ischemic myocardium using FGF-1 therefore antedates the November 4, 1997 filing date of Provisional Application No. 60/064,210, which discloses an increase in blood circulation to the myocardium by patent holes or injection into the myocardium with and without the use of angiogenic substances such as FGF-1.

7. Even as to those aspects of the invention that we conceived but had not reduced to practice at the reference date, we have worked diligently to achieve a constructive reduction to practice by preparing a patent application disclosing our invention in its entirety and filing that application on July 24, 1998 as Provisional application No. 60/093,962, six (6) months after the date of publication of the Schumacher et al. reference on February 24, 1998. The activity of drafting and filing a patent application demonstrates diligence from prior to the publication

of the cited reference on February 24, 1998, to a constructive reduction to practice July 24, 1998.

8. As a person signing below, I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States codes and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

Dated: May 05, 2002

By: _____
Thomas Stegmann, M.D.

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Prof. Dr. med. Th. Stegmann
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Stegmann, Thomas (as amended)
Appl. No.	:	10/649,480
Filed	:	August 27, 2003
For	:	METHOD OF PRODUCING BIOLOGICALLY ACTIVE HUMAN ACIDIC FIBROBLAST GROWTH FACTOR AND ITS USE IN PROMOTING ANGIOGENESIS
Examiner	:	Li, Bao Q
Group Art Unit	:	1648

DECLARATION OF INVENTORSHIP UNDER
In re Katz, 687 F. 2d 450, 215 U.S.P.Q. 14 (CCPA, 1982)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Thomas Stegmann, declare as follows:

1. I am the sole inventor of the claims of the above-identified patent application as amended in the accompanying Amendment, and am responsible for the inventive concepts disclosed therein.

2. I, am also one of the co-authors of the publication: B. Schumacher, MD; P. Pecher, MD; B.U. von Specht, MD; Th. Stegmann, MD, (1998) "Induction of Neoangiogenesis in Ischemic Myocardium by Human Growth Factors" Circulation vol. 97, pages 645-650, wherein significant aspects of the invention are described.

3. The following co-authors of the publication contributed to the study presented in the publication as follows, in terms of (a) the position held at the time of the study described in the publication; and (b) contribution to the work:

B. Schumacher, MD, (staff member & senior assistant in Department of Thoracic & Cardiovasular Surgery)

- assisted me during the coronary artery bypass graft (CABG) operations when intramyocardial FGF-1 injection was performed under my direct supervision
- performed collection and pre-evaluation of patient data under my supervision
- screened patients for the trial under my supervision
- collected data for the publication under my supervision

Peter Pecher, MD, **(staff member as non-certified cardiovascular surgeon)**

- collected patient data during the study
- provided surgical assistance in the operating room during the coronary artery bypass graft (CABG) operations while I performed the intramyocardial injection of FGF-1

B.U. von Specht, MD, **(employee of surgical research laboratory in Freiburg, Germany)**

- prepared FGF-1 used in the study following my instructions

4. The three co-authors listed above were involved only with providing assistance during the surgical procedures, screening patients for the study and preparation of the FGF-1 used in the study according to my directions. All three co-authors worked under my direct guidance and direction. They were not the inventors of the subject matter described in the patent application, but were listed as co-authors in order to receive credit for working on the project, as is the custom in scientific research programs.

5. For the reasons presented above, only myself, Thomas Stegmann, MD, who is listed as inventor on the above-referenced patent application is the true inventor of the subject matter claimed in the above-referenced application.

6. As a person signing below, I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States codes and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

Dated: August 22, 2005 By: _____

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Thomas Stegmann, MD